

THE DOUBLY LABELED WATER METHOD FOR MEASURING HUMAN
ENERGY EXPENDITURE: ADAPTATIONS FOR SPACEFLIGHT

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ABSTRACT

It is essential to determine human energy requirements in space and the doubly labeled water method has been identified as the most appropriate means of indirect calorimetry to meet this need. The method employs naturally occurring, stable isotopes of hydrogen (^2H , deuterium) and oxygen (^{18}O) which, after dosing, mix with body water. The deuterium is lost from the body as water while the ^{18}O is eliminated as both water and CO_2 . The difference between the two isotope elimination rates is therefore a measure of CO_2 production and hence energy expenditure.

Spaceflight will present a unique challenge to the application of the doubly labeled water method. Specifically, interpretation of doubly labeled water results assumes that the natural abundance or "background" levels of the isotopes remain constant during the measurement interval. This assumption does not hold true during spaceflight since the potable water on board the Space Shuttle, which is produced as a byproduct of electricity by the fuel cells, varies within the mission with respect to enrichment levels of these isotopes. Therefore, interpretation of doubly labeled water results during future in-flight studies will be complicated by the changing background isotope enrichments due to consumption of Shuttle water.

To address this issue an equilibration model will be developed in an on-going ground-based study. As energy requirements of women matched to counterparts in the Astronauts Corps are being determined by doubly labeled water, the baseline isotope concentration will be changed by consumption of "simulated Shuttle water" which is artificially enriched. One group of subjects will be equilibrated on simulated Shuttle water prior to energy determinations by doubly labeled water while the others will consume simulated Shuttle water after dosing. This process will allow us to derive a prediction equation to mathematically model the effect of changing background isotope concentrations.

The results of this study will inform us whether or not it will be necessary to initially equilibrate astronauts involved in future in-flight doubly labeled water studies with Shuttle water to prevent compromising interpretation of energy expenditure data. Since prior equilibration would be logistically difficult to accomplish, a mathematical model would significantly ease the technology involved in addressing the critical issue of human energy requirements in space.

INTRODUCTION

It is essential to determine human energy requirements in space to adequately assess food needs for long-term missions and to be able to predict energy requirements in closed ecological life support systems. The doubly-labeled water method has been identified by NASA as the most appropriate means of indirect calorimetry to meet this need. The method employs naturally occurring, stable isotopes of hydrogen (^2H , deuterium) and oxygen (^{18}O) which, after dosing, mix with the body water. Due to the action of the enzyme carbonic anhydrase, primarily in red blood cells, the isotopes equilibrate between water and carbon dioxide. The deuterium is then lost from the body as water while the ^{18}O is eliminated as both water and CO_2 . The difference between the two isotope elimination rates, determined from urine or saliva samples prepared for gas isotope ratio mass spectrometry, is therefore a measure of CO_2 production and hence energy expenditure.

The doubly labeled water method is considered a major advance in nutrition research because it allows for the quantification of energy expenditure in free-living populations for a period of days to weeks. There have already been many interesting applications of the method to address basic questions in nutrition science. For example, it has been applied to quantifying energy expenditure of people throughout the life cycle (1), including pregnant and lactating women (2). The doubly labeled water method has also been used to assess the energy cost of various work and exercise patterns (3) and in people in different environmental conditions (4). Given its potential use in such a variety of circumstances, it is essential to also understand its limitations. A number of investigators have probed the assumptions underlying the method to identify the conditions under which its validity and/or precision may be impaired and to develop the most accurate approaches to data analysis. The assumptions that underpin the doubly labeled water method include the following (5,6):

1. Body water is a single compartment that the isotopes (^2H and ^{18}O in H_2O) label and from which they are lost.
2. ^2H is lost only as water.
3. ^{18}O is lost both as water and as carbon dioxide; transference of oxygen between water and carbon dioxide is the consequence of a rapid exchange promoted by carbonic anhydrase.
4. Total body water, and output rates of water and carbon dioxide are constant.

5. Water and carbon dioxide losses occur with the same enrichment as that coexisting in body water.
6. Background isotope intake rates are constant.

In truth, none of these assumptions is absolute (5,6). Therefore, it is necessary to understand the significance of each of the model's imperfections in order to make the necessary corrections. This report will deal specifically with assumption number 6 because it is uniquely affected by space travel. Background concentrations of ^2H and ^{18}O are important considerations because in order to obtain data to calculate CO_2 production, the baseline value is subtracted from the post-dose enrichments. If the baseline value changes throughout the isotope disappearance curve and is unaccounted for, an error will be introduced into the final calculation.

Since stable isotopes occur naturally, they are in everything we eat, drink and breathe. Individuals thus take on a pattern of isotope enrichment that reflects their intake. With respect to ^2H and ^{18}O , the usual source of variation is brought about by evaporation and condensation processes where isotopic enrichment in humans follows the same pattern as that seen for water supplies, and ^2H and ^{18}O enrichments covary. There are several situations which have been shown to lead to changes in background enrichments. An obvious example would be a subject moving from one location to another and thereby changing his or her background intake. In addition, infants who are breastfed are more enriched than those who are bottle-fed (7); presumably at weaning breastfed babies become less enriched. Gambian infants have been found to have significant background variations at different times of the year (6). Finally, Jones et al. (8) have shown the effect of changing nutrition on background enrichments in infants weaned from total parenteral nutrition.

Spaceflight presents a new challenge for the doubly labeled water method, in particular for developing a systematic approach to dealing with changing background isotope enrichments. Currently, during spaceflight, the water which is consumed on board the Shuttle is produced as a byproduct of electricity by the fuel cells. The water varies within the mission with respect to enrichment levels of ^2H and ^{18}O . Therefore, interpretation of doubly labeled water data from inflight studies will be complicated by the changing background isotope enrichments due to consumption of Shuttle water. The study described below has been designed to address this issue.

PROCEDURES

The intent of the on-going project is two-fold: 1) to use the doubly labeled water method to determine energy requirements in lean, active women in the same age range as those in the Astronaut Corps, and 2) to alter conditions in this ground-based study to take into consideration changes in background isotope enrichment which will be involved in-flight due to consumption of Shuttle water.

A total of twelve women between the ages of 35 and 50, judged to be healthy by an Air Force Class 3 physical examination, will participate in the study. Weighed food records are being obtained throughout the study and exercise tests for maximal oxygen uptake and strength indicators are conducted at regular intervals. Body composition is assessed by skinfolds, underwater weighing, and bone densitometry. Resting energy expenditure is determined with a metabolic cart and canopy at the beginning and end of the doubly labeled water measurement of total energy expenditure.

The women are randomly assigned to two groups; group A has a changing baseline and group B has a stable baseline with respect to ^2H and ^{18}O . The baseline values are being manipulated by means of "simulated Shuttle water" which is intentionally enriched with the two heavy isotopes. Each subject obtains simulated Shuttle water from the Johnson Space Center and uses it for all food preparation and consumption throughout the energy expenditure assessment period. Women in group A are dosed with doubly labeled water simultaneously with initiation of consumption of simulated Shuttle water and therefore have a known change in the background enrichment of ^2H and ^{18}O . Women in group B consume simulated Shuttle water for two weeks prior to dosing with doubly labeled water. Urine samples are collected in this group both before and after dosing to quantify the change in baseline.

INTERPRETATION OF RESULTS

The data collected from the doubly labeled water procedure will be analyzed to determine total energy expenditure (TEE) for active women in this age range. The physical activity level (PAL) will also be assessed by dividing the TEE by resting energy expenditure (REE) measured by metabolic cart. This index ($\text{PAL} = \text{TEE} / \text{REE}$) is being increasingly used because it allows immediate comparison between subjects of different ages, sex, and body size, since the influence of these variables is largely removed by using REE as the denominator.

To address the issue of changing background enrichments, an equilibration model will be developed. Three factors will be considered to derive a prediction equation to mathematically model the effect of changing background isotope concentrations: the difference between measured baseline isotopic abundance and the predicted baseline on Shuttle water, the time interval of re-equilibration to the Shuttle water, and the fraction of water derived from the dietary source.

SIGNIFICANCE

The results of this study will provide important information on energy requirements of women aged 35 to 50. Data on normal, active women in this age group have been previously lacking. Since women represent an increasing proportion of the Astronaut Corps, these data will fill a void and improve estimates of food and oxygen needs for future flights.

The results of this study will also inform us whether or not it will be necessary to initially equilibrate astronauts involved in future in-flight doubly labeled water studies with Shuttle water to prevent compromising interpretation of energy expenditure data. Since prior equilibration would be logistically difficult to accomplish, a mathematical model would significantly ease the technology involved in addressing the critical issue of human energy requirements in space.

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